

INTRODUCTION TO  
***ADAPTIVE INTERVENTIONS***  
AND  
***SMART DESIGNS***

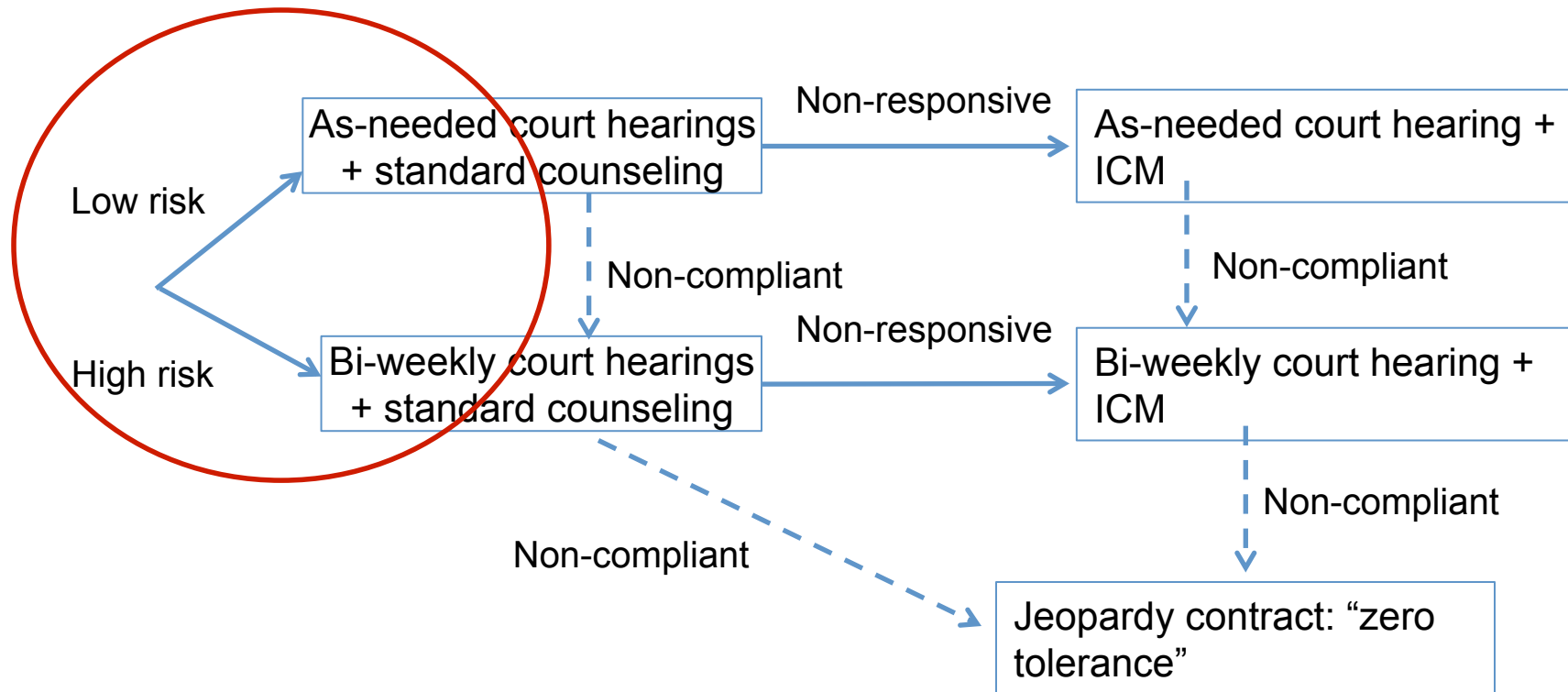
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Inbal (Billie) Nahum-Shani

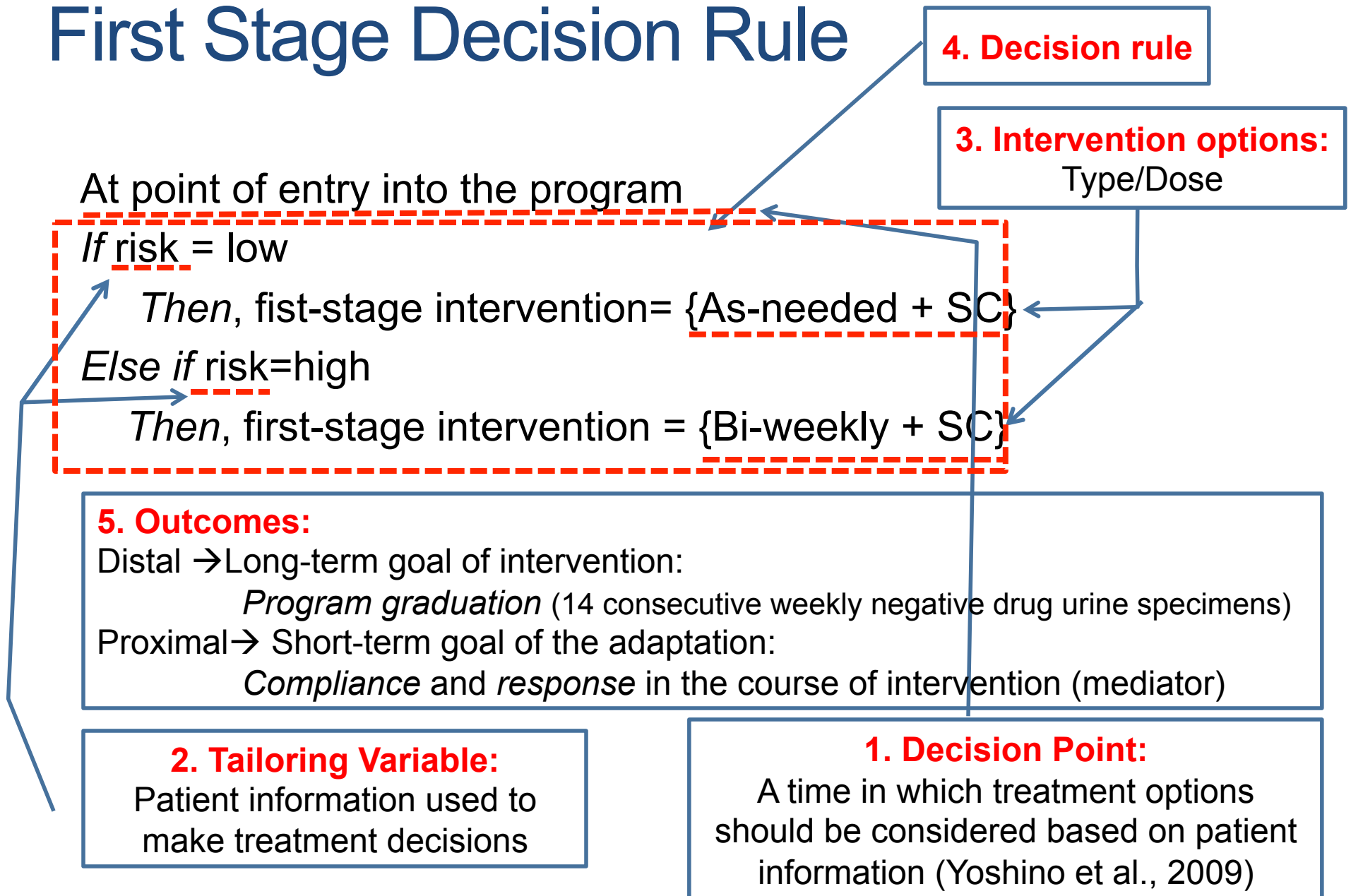
# Adaptive Interventions (AIs)

- Treatment design
  - Seeking to accommodate heterogeneity in response to treatment
  - Intervention options are adapted to the specific and changing needs of individuals
- Example (Marlowe et al., 2008; 2009; 2012)
  - Adaptive drug court program for drug abusing offenders
  - The goal: Minimize recidivism and drug use
    - Operationalized by graduating from the drug court program

# Adaptive Drug Court Program



# First Stage Decision Rule



# Adaptive Intervention: 5 Elements

1. **Decision Points** .....> **Trigger**
  2. Tailoring Variable .....> • Monitoring
  3. Decision rule .....> • Individualizing
  4. Intervention Options .....> • Delivering
  5. Proximal + Distal Outcomes .....> **Guide**
- } **Adaptation process**

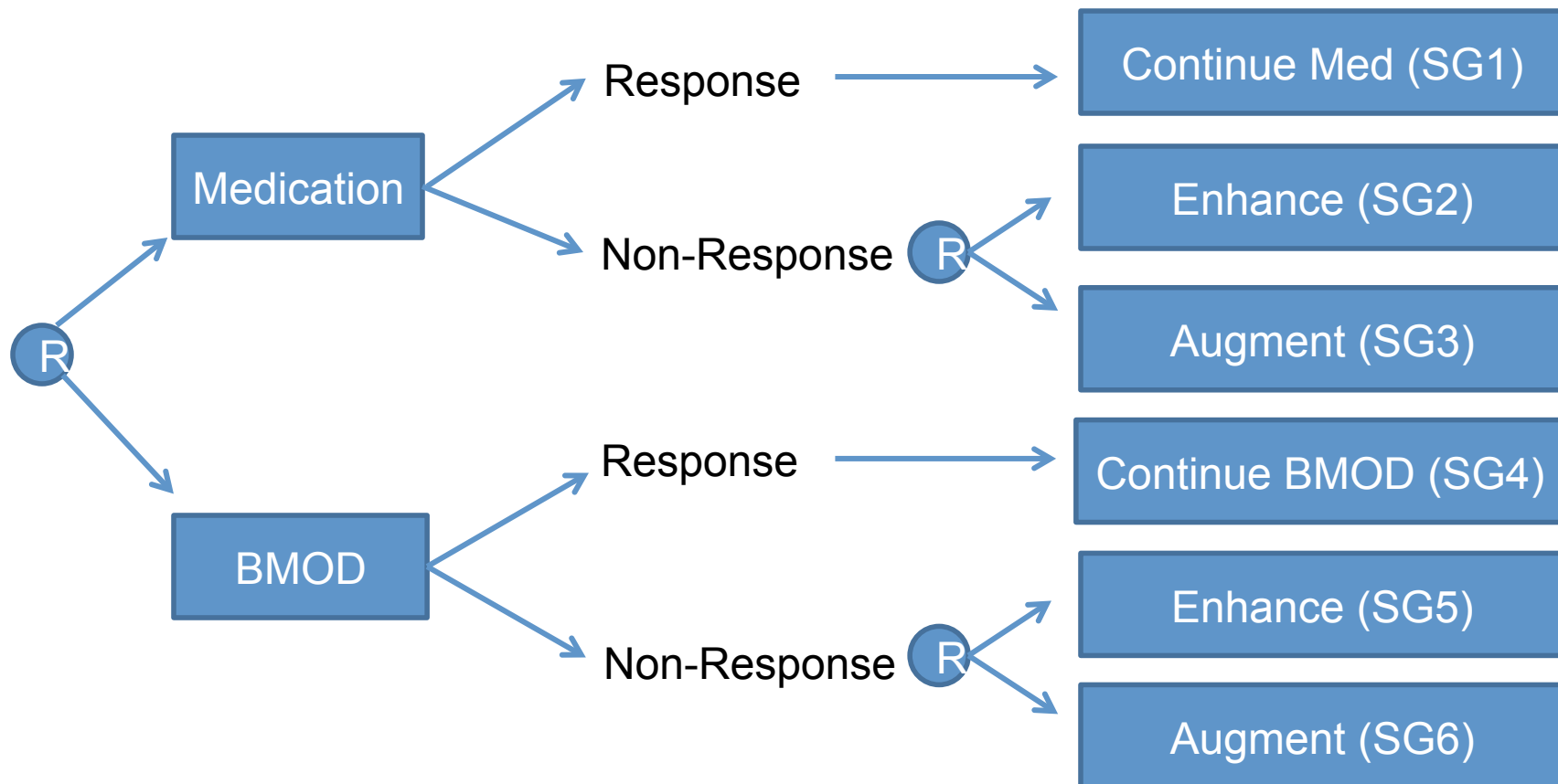
# SMART Designs

- To aid in constructing empirically-based AIs
- SMART:
  - Randomized Trials
  - Multiple stages of randomization
  - Each stage corresponds to a decision point

# Example

- Adaptive Interventions for Children with ADHD (Pelham)
- Motivation:
  - Debate about frontline treatment: **MED** or **BMOD**?
  - About 30% do not respond well to either MED or BMOD
    - What is the best “rescue” tactic:
    - **Enhance** intensity or **Augment** with the other type of treatment?

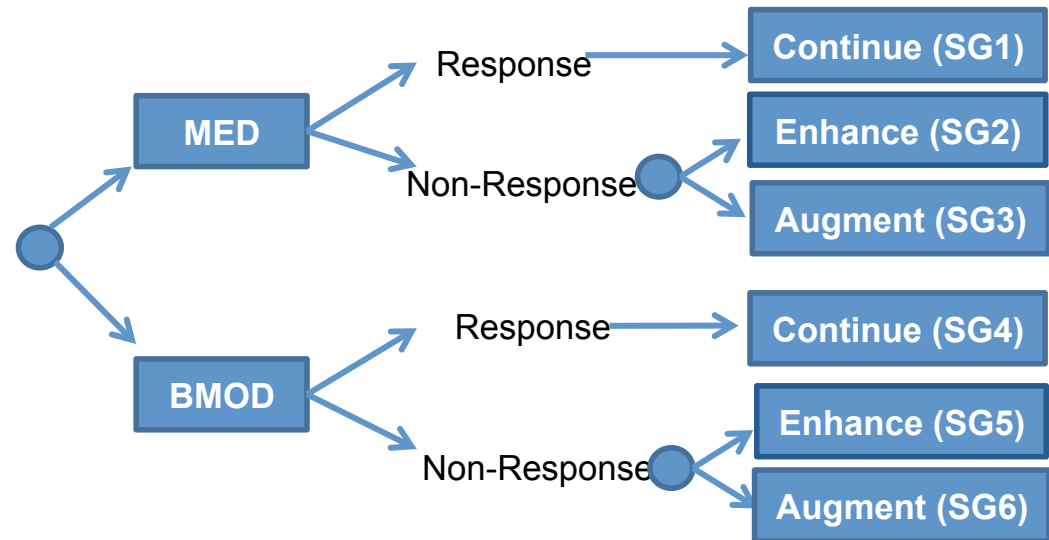
# ADHD SMART Study





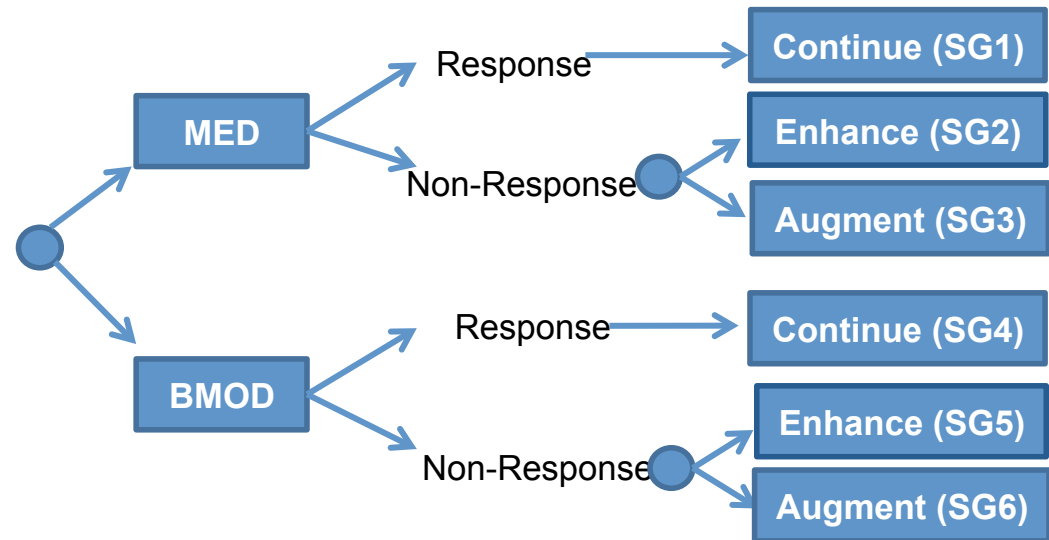
# Questions We Can Address with SMART

- **First-stage intervention options:**
- **Is it better to start with BMOD or MED?**
- **(SG1+SG2+SG3) vs. (SG4+SG5+SG6)**
- **Medication vs. BMOD**
  - Controlling for subsequent treatment



# Questions We Can Address with SMART

- **Second-stage intervention options:**
- **Is it better to Enhance or Augment for non-responders?**
- **(SG2+SG5) vs. (SG3+SG6)**
- **Enhance vs. Augment**



# Questions We Can Address with SMART

- **Embedded adaptive interventions**

*At the beginning of school year*  
 Stage 1 = {MED},  
 Then, every month  
 IF response = {NO}  
 THEN stage 2 = {AUGMENT}

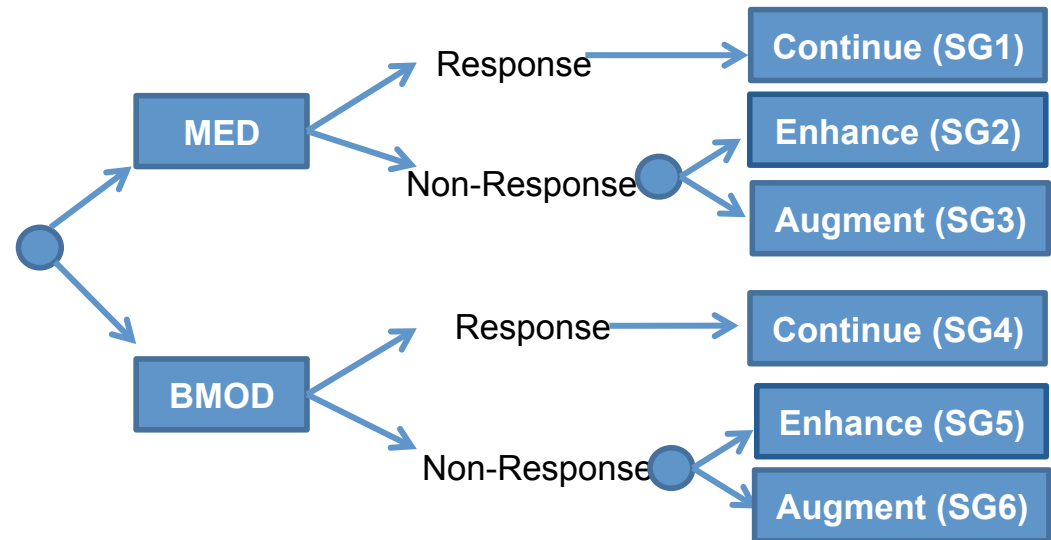
*At the beginning of school year*  
 Stage 1 = {MED},  
 THEN continue stage 1

Then, every month  
 IF response = {NO}  
 THEN stage 2 = {ENHANCE}  
 ELSE IF response = {YES}  
 THEN continue stage 1

*At the beginning of school year*  
 Stage 1 = {BMOD},  
 Then, every month  
 IF response = {NO}  
 THEN stage 2 = {ENHANCE}  
 ELSE IF response = {YES}  
 THEN continue stage 1

VS.

*At the beginning of school year*  
 Stage 1 = {BMOD},  
 Then, every month  
 IF response = {NO}  
 THEN stage 2 = {AUGMENT}  
 ELSE IF response = {YES}  
 THEN continue stage 1



# Results:

## Primary outcome:

- Children's school performance at month 8
- Based on the Impairment Rating Scale (IRS, Fabiano).
- Ranges from 1 to 5, with higher values= better school performance.

Adaptive intervention		Responders		Non-Responders		Estimated weighted mean	Robust SE
Stage 1	Stage 2	Sample size	Sample mean	Sample size	Sample mean		
<b>(1, -1)</b>	<b>BMOD AUGMENT</b>	<b>22</b>	<b>4.64</b>	<b>24</b>	<b>4.08</b>	<b>4.36</b>	<b>0.15</b>
<b>(-1, -1)</b>	<b>MED AUGMENT</b>	<b>36</b>	<b>4.39</b>	<b>17</b>	<b>3.47</b>	<b>4.00</b>	<b>0.15</b>
(1, 1)	BMOD INTENSIFY	22	4.64	22	3.96	4.17	0.22
(-1, 1)	MED INTENSIFY	36	4.39	18	4.22	4.27	0.13

# Primary Research Questions

1. Compare first stage intervention options
2. Compare second-stage intervention option
3. Compare embedded adaptive intervention

Nahum-Shani, I., Qian, M., Almirall, D., Pelham, W. E., Gnagy, B., Fabiano, G. A., ... & Murphy, S. A. (2012). Experimental design and primary data analysis methods for comparing adaptive interventions. *Psychological methods*, 17(4), 457.

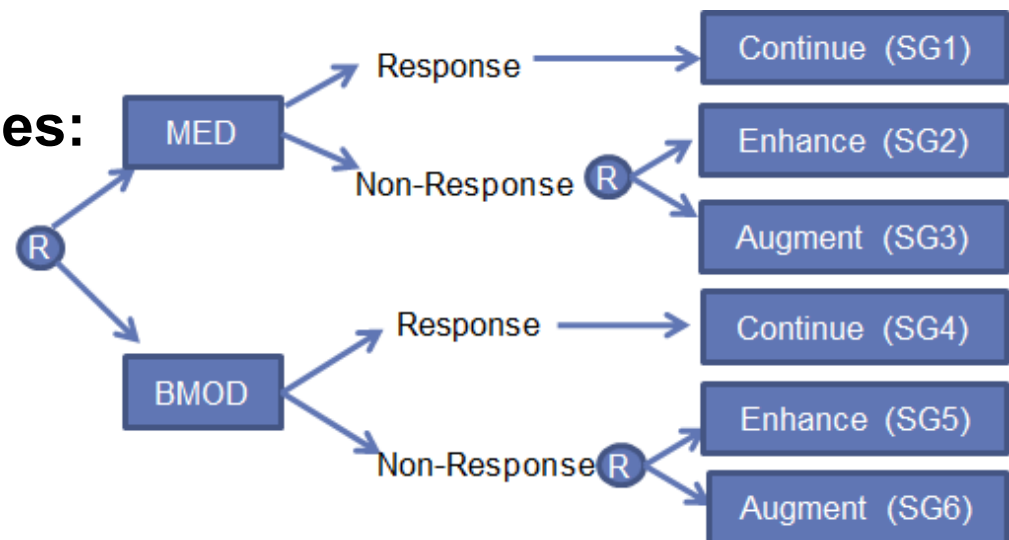
Oetting, A., Levy, J., Weiss, R., & Murphy, S. (2007). Statistical methodology for a SMART design in the development of adaptive treatment strategies. *Causality and Psychopathology: Finding the Determinants of Disorders and their Cures*. Arlington, VA: American Psychiatric Publishing, Inc.

# Exploratory Research Questions

- **More deeply tailored adaptive interventions.**
  - Using candidate tailoring variables *not embedded* in design.
- **Tailoring Variables?**
  - Strongly moderate the effect of intervention options, in a way which suggests that different intervention options should be offered depending on their values.

- **Candidate tailoring variables:**

- Medication prior to Stage 1
- Adherence to Stage 1



## More Deeply Tailored Decision Rule:

At the beginning of school year  
 IF **medication prior** to stage 1 = {NO-MED}  
     Stage 1 = {MED},  
     **THEN** stage 1 = {BMOD}.  
 Then, every month  
 ELSE stage 1 = {MED} or {BMOD}.  
 IF response = {NO}  
     **THEN** stage 2 = {AUGMENT}  
 Then, every month  
 ELSE IF response = {YES}  
     **THEN** continue stage 1  
 IF **response** to stage 1 = {NO}  
     **THEN IF adherence** to stage 1 = {LOW},  
         **THEN** stage 2 = {AUGMENT}.  
     **ELSE** stage 2 = {Augment} or {ENHANCE}.  
 ELSE continue stage 1.

# Q-learning (Watkins, 1989; Murphy, 2005)

- Popular method from computer science.
- Extension of moderated regression to sequential decision making
  - You use Q-learning by conducting a sequence of regressions.
  - One regression for each stage.
  - At each stage you:
    - Assess whether the candidate tailoring variable moderates the effect of the intervention options at this stage
    - In a way that is useful for making treatment decisions

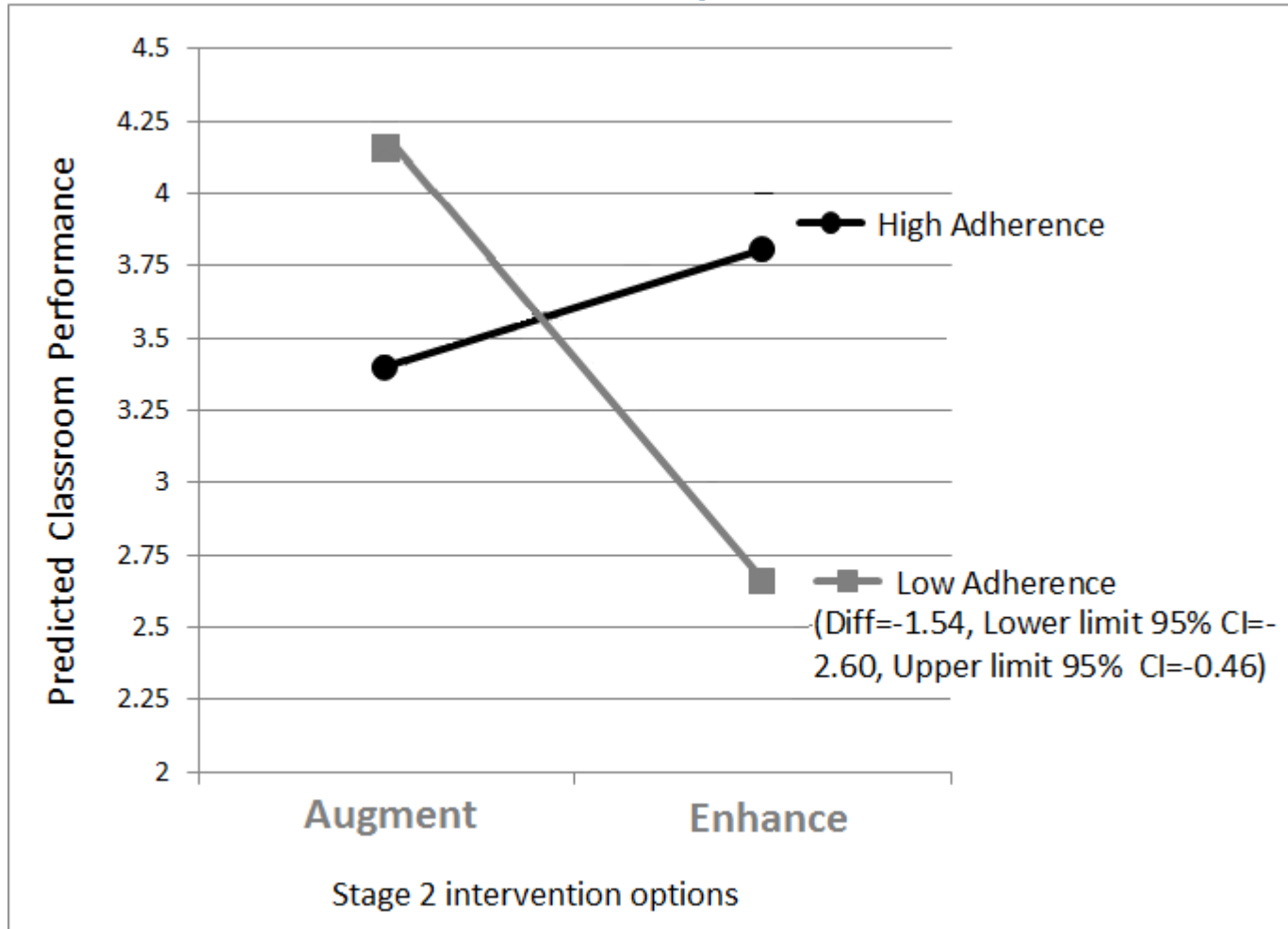
Nahum-Shani et al., (2012). Q-Learning: A Secondary Data Analysis Method for Developing Adaptive Interventions. *Psychological Methods*, 17(4), 478-494



## Stage 2:

Regress Y on **O1**, **A1**, **O2**, **A2**, **O2\*A2**

Best tactic for non-responders, given adherence



# Learn More

- Websites with resources:
  - Methodology Center: <http://methodology.psu.edu/ra/adap-inter/projects>
- Key ideas:
  - Murphy, S. A., (2005). An experimental design for the development of adaptive treatment strategies. *Statistics in Medicine*, 24(10), 1455–1481.
  - Murphy, S. A. (2003). Optimal dynamic treatment regimes. *Journal of the Royal Statistical Society, Series B*, 65(2), 331-366.
- Overview of completed or ongoing SMART studies:
  - Lei, H., Nahum-Shani, I., Lynch, K., Oslin, D., & Murphy, S. A. (2012). A "SMART" design for building individualized treatment sequences. *Annual Review of Clinical Psychology*, 8, 14.1 - 14.28.
- Introduction to SMART
  - Almirall D., Nahum-Shani, I., Sherwood, N.E., Murphy S.A. (accepted 2014, in press). Introduction to SMART Designs for the Development of Adaptive Interventions: With Application to Weight Loss Research. *Translational Behavioral Medicine*.



# Thank you!

- Email me questions/comments: [Inbal@umich.edu](mailto:Inbal@umich.edu)
- Collaborators:
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    - Susan Murphy: <http://dept.stat.lsa.umich.edu/~samurphy/>
    - Danny Almirall: <http://www-personal.umich.edu/~dalmiral/>
    - Linda Collins: <http://methodology.psu.edu/people/lcollins>